REMARKS

Claims 90-96 and 113-131 are pending in the application. In the office action mailed June 8, 2009, claims 90-96 and 113-131 are rejected. Consideration of the following remarks is respectfully requested.

Claims 90-96 and 113-131 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. patent No. 6,322,819 ("Burnside") in view of U.S. patent No. 4,326,525 ("Swanson").

The pending claims are directed to a pharmaceutical dosage form comprising a gastric retention vehicle composition comprising superdisintegrant, tannic acid, and hydrogel. The gastric retention vehicle composition is *a homogenous solid matrix*, in which the first and second particles containing methylphenidate are dispersed. The gastric retention vehicle composition comprises about 10 wt-% to about 75 wt-% superdisintegrant, about 2 wt-% to about 12 wt-% tannic acid, and about 20 wt-% to about 70 wt-% of hydrogel. The second particles are coated with a coating that is impermeable to methylphenidate and dissolves in gastric fluid, and, after a sufficient amount of the coating is dissolved, the methylphenidate is released from the second particles into the stomach. Upon contact with gastric fluid, the gastric retention vehicle composition expands to a sufficient degree such that the dosage form is retained in the stomach at least until methylphenidate is released from the second particles. As Applicants have shown, the amounts of hydrogel, superdisintegrant, and tannic acid affect the expansion and strength of the dosage form (see, e.g., Examples 1, 2 and 3 of the present application; and the Declaration by Vered Rosenberger submitted on March 16, 2009). The presently claimed compositions, by using the claimed amounts of hydrogel, superdisintegrant, and tannic acid, achieve the goal of gastric retention.

In contrast, Burnside teaches a multiple pulsed dose drug delivery system for pharmaceutically active amphetamine salts, comprising an immediate-release component and an enteric delayed-release component wherein (1) the enteric release coating has a defined minimum thickness and/or (2) there is a protective layer between the pharmaceutically active amphetamine salt and the enteric release coating and/or (3) there is a protective layer over the enteric release coating (*see, e.g.*, Burnside, Abstract). Burnside teaches that its drug delivery system is in the form of a pellet or beadlet comprising a core, drug layer(s) and coating layer (s) (*see, e.g.*, Burnside, Fig. 2A). Although Burnside teaches that a binder and a disintegrant

may be used in its drug delivery system, they are used to form a coating layer over a drug layer rather than to form a homogeneous matrix in which the drug particles are dispersed.

Burnside teaches that its pellets can be incorporated into a tablet matrix (*see, e.g.*, Burnside, col. 9, ll. 27-46). Burnside teaches that a binder and a disintegrant may be used for its tablet matrix. However, Burnside explicitly teaches that its tablet matrix "rapidly disperses the particles after ingestion" (Burnside at col. 9, ll. 27-29), and that the disintegrant is added "in order to disperse the beads once the tablet is ingested" (Burnside at col. 9, ll. 40-42).

Thus, Burnside does not teach or suggest gastric retention of its drug. Instead, Burnside teaches that its delayed release component is designed not to be released in the upper gastrointestinal tract but in the intestine (*see, e.g.*, Burnside, col. 4, ll. 18-31; col. 5, ll. 54-63). Burnside does not teach or suggest a gastric retention matrix which retains the dosage form in the stomach at least until methylphenidate is released from the second particles. Burnside does not teach or suggest including tannic acid in its drug delivery system or its tablet matrix. Nor does Burnside teach or suggest the effects of the amounts of tannic acid, hydrogel and superdisintegrant on the expansion and strength of the formulation.

Swanson teaches an osmotic device comprising an agent and a buffer, which interact in the device to produce an agent with controlled solubility in the fluid (*see, e.g.*, Swanson at col. 2, lines 40-49). The buffer can be, *inter alia*, an acidic compound that is capable in an aqueous solution of reacting with a counter basic agent to produce an aqueous soluble agent salt within the device for dispensing the agent salt at a substantially zero order rate from the device over time (*see, e.g.*, Swanson at col. 7, lines 21-29). Swanson teaches that the preferred acidic compounds are fumaric acid, succinic acid, tartaric acid, citric acid, maleic acid, benzoic acid, ascorbic acid, oxalic acid, nicotinic acid, lactic acid, phthalic acids, pimaric acid, pimelic acid, tannic acid, urea hydrochloride, glycine, mandelic acid, glycolic acid, sodium monobasic phosphate, potassium bisulfite, potassium monobasic phosphate, and the like (*see, e.g.*, Swanson at col. 7, lines 39-47). Thus, Swanson teaches the inclusion of an acid in its device for reacting with a base to produce a salt, not for enhancing the expansion and strength of a matrix. Swanson teaches as preferred acids a long list of over twenty acids, with tannic acid as but one of the list.

The Federal Circuit recently stated in *Eisai Co. Ltd. v. Dr. Reddy's Laboratories, Ltd.*

> [i]n *KSR*, the Supreme Court noted that an invention may have been obvious "[w]hen there [was] ... a design need or market pressure to solve a problem and there [were] ... a finite number of identified, predictable solutions." 127 S.Ct. at 1742 (tense changes supplied to clarify, as the Court stated and as per 35 U.S.C. § 103, that the obviousness inquiry must rely on evidence available "at the time" of the invention, see *Takeda*, 492 F.3d at 1356 n. 2). The Supreme Court's analysis in *KSR* thus relies on several assumptions about the prior art landscape. *First, KSR assumes a starting reference point or points in the art, prior to the time of invention, from which a skilled artisan might identify a problem and pursue potential solutions. Second, KSR presupposes that the record up to the time of invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound. ... Third, the Supreme Court's analysis in KSR presumes that the record before the time of invention would supply some reasons for narrowing the prior art universe to a "finite number of identified, predictable solutions,"* 127 S.Ct. at 1742. *In Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.*, 520 F.3d 1358, 1364 (Fed.Cir.2008), this court further explained that this "easily traversed, small and finite number of alternatives ... might support an inference of obviousness." To the extent an art is unpredictable, as the chemical arts often are, *KSR*'s focus on these "identified, predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable.

Eisai Co. Ltd. v. Dr. Reddy's Laboratories, Ltd. 533 F.3d 1353, 1359 (Fed. Cir. 2008); Rehearing and Rehearing *En Banc* Denied Sept. 16, 2008 (emphasis added). In the present case, neither Burnside nor Swanson teaches or suggests the problems associated with conventional gastric retention compositions, such as slow expansion and low strength. Applicants note that neither Burnside nor Swanson is concerned with a gastric retention composition. Neither Burnside nor Swanson teaches or suggests, *inter alia*, that the amounts of disintegrant, tannic acid, and hydrogel affect the expansion and strength a gastric retention composition.

Neither Burnside nor Swanson provides a reason why a person skilled in the art would have desired to modify Burnside by adding tannic acid to either its coating layer or tablet matrix. In this regard, Applicants respectfully point out that, as discussed above, Burnside explicitly teaches that its drug delivery system is for releasing the drug in the intestine rather than the upper gastrointestinal tract. Neither Burnside nor Swanson provides a reason why a

person skilled in the art would have not only selected from Swanson's disclosures of different buffer compounds an acid but also selected tannic acid out of the long list of acids. Neither Burnside nor Swanson provides a reason why a person skilled in the art would have added tannic acid to disintegrant and hydrogel in the recited amounts to obtain a gastric retention vehicle with enhanced expansion and strength. In the office action, the Examiner essentially suggests that because Burnside teaches a formulation of methylphenidate comprising hydrogel and disintegrant, and Swanson teaches a formulation of methylphenidate which may contain tannic acid, a gastric retention vehicle composition containing hydrogel, disintegrant, and tannic acid in the recited amounts for enhanced expansion and strength is obvious. However, as discussed above, Burnside teaches that its tablet matrix comprising hydrogel and disintegrant rapidly disperses the drug particles after ingestion, while Swanson teaches including tannic acid in an osmotic device as buffer for reacting with a base to produce a salt. The mere fact that a formulation of methylphenidate comprising hydrogel and disintegrant and a formulation of methylphenidate which may contain tannic acid are separately known in the art does not provide a reason for a person skilled in the art to combine hydrogel, disintegrant, and tannic acid, much less in the recited amounts to obtain a gastric retention vehicle with enhanced expansion and strength.

Furthermore, neither Burnside nor Swanson provides what a person skilled in the art would have expected or predicted to achieve by adding tannic acid to Burnside's coating layer or tablet matrix. As discussed above, Burnside's coating layer is not a matrix in which drug particles are dispersed, while Burnside's tablet matrix rapidly disperses the drug particles after ingestion. Swanson teaches including tannic acid as a buffer for reacting with a base to produce a salt. Thus, a person skilled in the art would not have expected or predicted that adding tannic acid to Burnside's coating layer or tablet matrix would have turned such it into a gastric retention vehicle which retains methylphenidate in the stomach at least until methylphenidate is released from the second particles.

Therefore, for at least the above reasons, Burnside and Swanson, alone or in combination, do not support a case of obviousness.

In addition, with respect to its delayed-release component, Burnside explicitly teaches that it is designed not to be released in the upper gastrointestinal tract but in the intestine, whereas with respect to its tablet matrix, Burnside explicitly teaches that it "rapidly disperses

the particles after ingestion", and that the disintegrant is added to the tablet matrix "in order to disperse the beads once the tablet is ingested". Thus, even if assuming, *arguendo*, a person skilled in the art would have added tannic acid to either Burnside's coating layers or Burnside's tablet matrix, it would have led to a composition for gastric retention, which would not have satisfied Burnside's own purpose of delayed release of the drug in the intestine.

Applicants further respectfully submit that the Examiner's contention is based on hindsight reconstruction. As discussed above, in order to arrive at the presently claimed invention as the Examiner has suggested, a person skilled in the art would have to first pick Burnside's formulation designed for delayed release of a drug in the intestine, then select from amongst all of the buffer compounds, and the laundry list of acids, of Swanson, tannic acid, and finally to combine tannic acid in the recited amount with Burnside's composition. As discussed above, neither Burnside nor Swanson provides a reason why a person skilled in the art would have carried out such picking/selecting/adding. Only with the assistance of hindsight, can the Examiner arrive at the presently claimed invention by the proposed modification of Burnside in view of Swanson. In *Sanofi-Synthelabo, Inc., v. Apotex, Inc.*, the Federal Circuit has stated that

> [t]he application of hindsight is inappropriate where the prior art does not suggest that this enantiomer could reasonably be expected to manifest the properties and advantages that were found for this particular dextrorotatory isomer. *See Graham*, 383 U.S. at 36, 86 S.Ct. 684 (*cautioning against hindsight whereby the teachings of the invention are read into the prior art*); see also *KSR v. Teleflex*, 127 S.Ct. at 1742 (*recognizing "hindsight bias" and "ex post reasoning" as inappropriate in determination of obviousness*).

Sanofi-Synthelabo, Inc., v. Apotex, Inc., 550 F.3d 1075 (Fed. Cir. 2008); Rehearing and Rehearing *En Banc* Denied March 26, 2009 (emphasis added).

Claims 90, 93, 116 and 117 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Burnside in view of Swanson in further view of U.S. patent no. 5,874,090 ("Baker"). The Examiner indicates that claims 90 and 93 are rejected as being obvious over Burnside in view of Swanson, while Baker is cited for its teaching that methylphenidate can be used to treat hyperactivity. As discussed above, the pending claims are not obvious over Burnside and Swanson. Since Baker does not teach inclusion of hydrogel, superdisintegrant,

and tannic acid in its formulation, Baker does not supply what is missing in Burnside and Swanson with respect to claims 90 and 93. Although Baker generally discloses that the methylphenidate formulation may be in matrix, coating, reservoir, osmotic, ion-exchange or density exchange form, it fails to disclose a gastric retention vehicle comprising superdisintegrant, tannic acid, and hydrogel, much less a gastric retention vehicle comprising these components in the amounts recited in the claims for enhanced expansion and strength. Claims 116 and 117 are method claims dependent on claims 90 and 93, respectively. Since the base claims 90 and 93 are not obvious over Burnside, Swanson and Baker, claims 116 and 117 are also not obvious.

For at least all of the above reasons, Applicants respectfully submit that claims 90-96 and 113-131 are not obvious over Burnside and Swanson, alone or in combination; and claims 90, 93 and 116-117 are not obvious over Burnside, Swanson and Baker, alone or in combination. The rejections of these claims under 35 U.S.C. § 103(a) should be withdrawn.

In view of the foregoing amendments and remarks, Applicants respectfully submit that the present application is in condition for allowance. Early and favorable action by the Examiner is earnestly solicited. If any outstanding issues remain, the examiner is invited to telephone the undersigned at the telephone number indicated below to discuss the same.

In the event that the filing of this paper is deemed not timely, applicants petition for an appropriate extension of time. The Office is authorized to charge any underpayment or credit any overpayment to Kenyon & Kenyon LLP's Deposit Account No. 11-0600.

Respectfully Submitted,

KENYON & KENYON

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